

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 980057.415PC	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. PCT/US2004/024658	International filing date ( <i>day/month/year</i> ) 29 July 2004 (29.07.2004)	Priority date ( <i>day/month/year</i> ) 30 July 2003 (30.07.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant XENON PHARMACEUTICALS INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

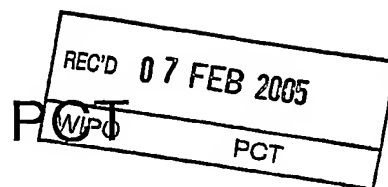
- |  |   |
|--|---|
| <input checked="" type="checkbox"/> Box No. I    | Basis of the report   |
| <input checked="" type="checkbox"/> Box No. II   | Priority  |
| <input checked="" type="checkbox"/> Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/> Box No. IV              | Lack of unity of invention  |
| <input checked="" type="checkbox"/> Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> Box No. VI   | Certain documents cited   |
| <input checked="" type="checkbox"/> Box No. VII  | Certain defects in the international application  |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Date of issuance of this report 30 January 2006 (30.01.2006)
	Authorized officer  <b>Dorothee Mülhausen</b>  Telephone No. +41 22 338 87 40

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY



To:

10/2

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2004/024658

International filing date (day/month/year)  
29.07.2004

Priority date (day/month/year)  
30.07.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D239/42, C07D241/26, A61K31/497, A61K31/506, A61P3/06

Applicant  
XENON PHARMACEUTICALS INC.

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/024658

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/024658

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**Box No. II    Priority**

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1. ☐ The following document has not been furnished:

- ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/024658

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 1-9,27,36,44,50

because:

- ☒ the said international application, or the said claims Nos. 1-9,27,36,44,50 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/024658

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	8-45,47-50
	No: Claims	1-7,46,51
Inventive step (IS)	Yes: Claims	10-45,47-50
	No: Claims	1-9,46,51
Industrial applicability (IA)	Yes: Claims	10-26,28-35,37-43,45-49,51
	No: Claims	

2. Citations and explanations

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

**see form 210**

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

**see separate sheet**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/024658

- 1) The present application relates to (piperazin-1-yl)-pyrimidine and -pyrazine derivatives having human stearyl-CoA desaturase inhibiting activity.

- 2) Cited documents:

D1: WO 01/96327 A1

D2: WO 02/10154 A2

D3: DE 23 41 925 A1

D4: TETRAHEDRON, 53(18),1997, pages 6421-6432

D5: WO 01/62954 A2

D6: WO 03/091247 A2

D7: WO 03/075929 A1

Document D6 and D7 were published after the claimed priority; on the presumption that the priority is valid, these documents are not considered as prior art.

- 3) Novelty

D1 already describes heterocyclic amides as apolipoprotein B inhibitors, which seems to anticipate the subject-matter of claims 1-7 (see indications page 1, general formulae page 4 and claim 1).

D2 already describes heterocyclic amides which inhibit factor Xa, which seems to anticipate the subject-matter of claims 1-3 (see general formula claim 1, examples, see indications claims 18-20)

D3 describing hypotensive and antithrombotic pyrimidines seems to anticipate the subject-matter of claims 46 and 51 (see intermediate examples on pages 20-21).

D4 describes a metabolite covered by claim 46 (see page 8422 compound 11d).

D5 describes assays for identifying stearyl-CoA desaturase inhibitors, not however the presently defined compounds.

- 4) Inventive step

In as far as the subject-matter is novel, the following observations apply to the requirement of inventive step:

In as far as claims 1-9 relate to the application of compounds covered by the general formula described in document D1 it is noted that the mere fact that the present application identifies stearyl CoA desaturase inhibition as a mechanism does not seem to affect the clinical applications covered by these claims.

Accordingly, these claims seem in part to merely define the use of defined compounds for the treatment of disorders for which the compounds had in part already generally been indicated as useful in D1. Such selection would seem obvious to the person skilled in the art.

In as far as the claims relate to new compounds or specific new applications of such compounds (in as far as not covered by D1) an inventive step seems in principle acceptable, as no prior art suggests the defined compounds as solution to the problem of providing further stearyl Co-A desaturase inhibitors.

5) Further observations

Claims 1-9,27,36,44 and 50 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Claim 2 seems to fall within the scope of claim 1 and should therefore be dependent on claim 1.

Inhibition of stearyl-CoA desaturase reflects a mechanism of action rather than a clear therapeutical application.

The claims comprise implicitly (e.g. alkyl etc. may be optionally substituted see page 11 and following) and explicitly (e.g. multiring, aryl) opened features; with such opened features subject-matter is comprised that is unlikely to solve any relevant technical problem.

Claims 1, 10, 29, 38 and 46 comprise various proviso's; should these proviso's exclude prior art, such prior art is to be mentioned in the description.